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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,677	10/28/2005	Leena Otsomaa	06267.0130	8394

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EXAMINER	
ROBINSON, BINTA M	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 11/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/541,677	OTSOMAA ET AL.	
	Examiner	Art Unit	
	Binta M. Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *2-6, 10* is/are allowed.

6)☒ Claim(s) *1 and 7-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/8/05;10/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Claims 2-6, and 10 are allowable.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koskelainen et. al. based on the 102 (e) date of the reference.

Koskelainen et. al. discloses the compound, 5-Nitro-2-(2-phenylindan-5-yloxy) pyridine. At page 46, see the Koselianen compound

The difference between the prior art compound and the instantly claimed compound is the point of attachment of the oxy moiety to the pyridine ring. In the instant compound, the oxygen is attached to the pyridine ring at the 3, 4, or 5 position. In the prior art compound, the oxygen is attached at the pyridine ring at the 2 position. The Koskelainen compound, which has pharmaceutical activity as a NA+/CA2+ inhibitor is a positional isomer of the instant compound.

It would have been obvious to one of ordinary skill in the art to modify the prior art compound in order to create a positional isomer of it. Accordingly, the compounds are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds over those of the generic prior art compounds.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 10482396 (PGPub 20040235905). Although the conflicting claims are not identical, they are not patentably distinct from each other because the application claims a genus of compounds, pharmaceutical compositions, and methods of treating which overlap in subject matter with the instant genus of compounds, pharmaceutical compositions and methods of treating.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Application 10482396 teaches the instant compound as shown in Formula I, wherein X is O, CH2, or –C(O)-, Z is –CHR9 or valence bond, Y is –CH2, -C(O)-, CH(OR10), O, S, provided that in case Z is a valence bond, Y is not C(O); the dashed line represents an optional double bond in which case Z is –CR9 and Y is –CH-,

C(OR10)-, R1 is pyridinyl(R6), R2 and R3 are independently H, lower alkyl, lower alkoxy, -NO2, halogen, CF3, OH, NHR8, or –COOH, R6 is –NO2, R9 is H or lower alkyl, R10 is H, alkylsulfonyl or acyl, R14 and R19 are independently H, acyl, alkylsulfonyl, C(S)NHR17 or C(O)NHR17, R17 is H or lower alkyl. At claim 1, see pages 88-89. The difference between the prior art genus of compounds, pharmaceutical compositions and methods of treating and the instant genus, pharmaceutical compositions and methods of treating is that the prior art genus overlaps in subject matter with the instant genus of compounds, compositions, and methods of use.

The patentee teaches a very limited number of selections for the variables of this genus that are small enough in number to be combined to form the instant genus. Since the patentee teaches a small group of compounds within a genus that overlaps in subject matter with the instant genus, it would have been obvious for one of ordinary skill in the art to easily envision and test the compounds that overlap with the prior art genus of compounds. Accordingly, the compounds, compositions, and methods of use of these compounds are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds, compositions and methods of use over those of the generic prior art compounds, compositions and methods of use.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The Nature of the Invention

The nature of the invention in claims is a pharmaceutical composition for use in treating arrhythmas, as well as a method of treating arrhthmias with the instant compound.

The State of the Prior Art

The state of the prior art is that the Na+/Ca2+ exchange mechanism is one of the ion transport mechanisms that regulate the concentration of sodium and calcium ions in the cells. Compounds which selectively inhibit Na/Ca2+ exchange mechanism and thereby prevent overload of Ca2+ in cells are regarded as useful in preventing the cell injury mechanism of cardiac muscle and the like after ischemia and reperfusion. See lines 14-22 on page 1.

The predictability or lack thereof in the art

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of Na+/Ca2+ exchange mechanism-mediated diseases, whether the exchange mechanism was inhibited or not would affect the possible treatment of any disease.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the compound of claim 1 and the inhibition of the Na+/Ca2+ mechanism, one of skill in the art is unable to fully predict possible results from the administration of the compound of claim 1 due to the unpredictability of the role of this mechanism, i.e. whether or not inhibition would be beneficial for the treatment of the diseases.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present

The direction present in the instant specification is that the compounds of claim 1 can inhibit the the Na+/Ca2+ exchange mechanism which helps in the treatment of arrhythmias. However, the specification is fails to provide guidance as to whether the diseases disclosed the inhibition of this exchange mechansim.

The presence or absence of working examples

There are no working examples for any other diseases listed in the specification. Also, the compounds which are discloses in the specification have no pharmacological data regarding the treatment of any other disease. Also, the specification fails to provide working examples as to how the listed diseases can be treated by the inhibition of the exchange mechanism

The breadth of the claims

The breadth of the claims is that the compound of claim 1 can treat any arrhythmia.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what listed diseases would be benefited by the inhibition of Na+/Ca2+ exchange mechanism and would furthermore then have to determine whether the claimed compounds would provide treatment of the disease by the inhibition of Na+/Ca2+ exchange mechanism.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the claim 1 for the treatment of an Na+/Ca2+ exchange-mediated disease. As a result necessitating one of skill to perform an exhaustive search for which Na+/Ca2+ exchange -mediated diseases can be treated by the compound of claim 1 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which Na+/Ca2+ exchange -mediated diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Thomas McKenzie can be reached on 571-272-0670.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-1600.

THOMAS MCKENZIE, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

BMR
October 27, 2006